Carbon ion induced vascular damage in the rat lung*

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Introduction

Bronchial carcinomas are one of the most frequent causes of death in Germany. Radiotherapy is used in progressed stages of the cancer if the tumor cannot be removed surgically. The aim of radiotherapy is to control tumor growth by the administration of a high dose while the normal tissue surrounding the tumor is intended to be spared. Charged particles have the beneficial feature of an inverse depth dose distribution which means that the normal tissue can be spared while a high dose is absorbed by the tumor [1]. However, doses to the healthy tissue may be high enough to provoke side effects like pneumonitis or fibrosis. These effects are preceded by vascular damage, which is considered to be related to the pathogenesis of pneumonitis and fibrosis [2]. Here we investigated the impact of Carbon ions on blood vessel damage in the rat lung.

Materials and Methods

Lungs of adult male albino Wistar rats were irradiated with 270 MeV/u Carbon ions. Either 100% of lungs were irradiated (8.5 Gy or 12.5 Gy) or 50% (17.25 Gy) as described in [3]. After 8 weeks animals were sacrificed and lungs embedded in paraffin. Lung slices were stained with Verhoeff-van-Gieson staining, which allows distinguishing the different layers of a blood vessel. Vessel occlusion was determined by calculating the ratio of the thickness of the *Tunica media* to the diameter of the *Membrana elastica externa*. Only vessels with a maximum diameter of 50 μm and round shape were considered. Analysed vessels of 50% irradiated lungs were located exclusively in irradiated areas of the lungs.

Results and Discussion

A thickening of the vessel wall, mainly of the *Tunica media*, was observed after irradiation, which led to an occlusion of the blood vessel (Fig. 1). A higher dose induced a more pronounced occlusion of the blood vessels in comparison to a lower dose of Carbon ions (Fig. 2A). Interestingly, a higher irradiation volume had, despite the lower local dose, a stronger effect on the induced vessel occlusion than a smaller irradiation volume (Fig. 2B).

These results show for Carbon ions similar effects already reported for protons to blood vessels in the lung [4], which show that a low dose administered to a large volume is more efficient than a high dose to a small volume. The thickening of the vessel wall is probably due to an increased proliferation of smooth-muscle cells (SMC) that form the *Tunica media*, but potentially also due to an invasion of SMC into the *Tunica intima*. It was already shown that irradiated endothelial cells enhance the proliferation of SMC [5].

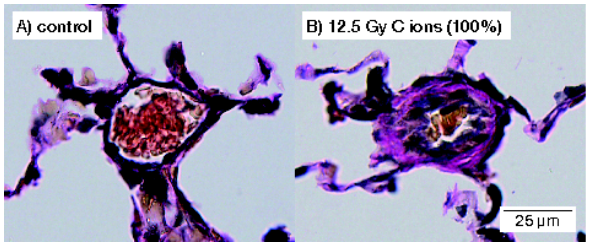

Figure 1: Representative example of a normal blood vessel (A) in comparison to an irradiated vessel 8 weeks after irradiation with Carbon ions (B).

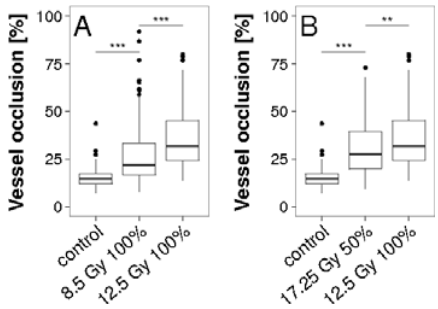

Figure 2: Vessel occlusion in the rat lung 8 weeks after irradiation with Carbon ions. Either the whole lung was irradiated (8.5 Gy and 12.5 Gy) or only 50% of the lung. Panel A shows the dose effect and panel B the volume effect.

References

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* Supported by HGS-HIRe and grant CBR-754842 from the University of Groningen

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